[ID-P#036] Exploring the Anticancer Potential of Snake Venom L-Amino Acid Oxidase (SV- LAAO) In Glioblastoma Multiforme: In Silico and In Vitro Analysis

Shankar Bakkannavar[a]; Divya Ramesh[a]; Dr. Vinutha Bhat[a] and Shreedhar Pai[b]
[a]Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal; [b]Manipal College of Pharmaceutical Sciences, Manipal, Manipal Academy of Higher Education, Manipal

Objective: The study aimed to investigate the anticancer potential of Snake venom L amino acid oxidase by in silico and in vitro methods.

Methodology: Protein-Protein interaction was checked between Snake venom LAAO(SVLAAO) and overexpressed proteins of Glioblastoma using Schrodinger software. The proteins were prepared using Schrödinger module using protein preparation wizard and optimization by OPLS3E force field.1 Docking was done between ligand and receptor. In vitro Cytotoxicity was done by SRB assay to check cytotoxicity of the SVLAAO and C6 glioma cells. C6 cells were cultured in 96 wells plate. These cells were treated with 10uM of SVLAAO, and serial dilutions were performed to determine IC50. After incubation, TCA was added to the wells for fixation.100µl SRB dye was added to wells and incubated for 30minutes, and OD measured at 540nm.2

Results: The Protein-Protein interaction was analysed using various parameters such as distance between residues, interactions, or clashes if present, hydrogen bonds, salt bridges, Pi stacking, Vander walls clashes, Buried SASA and surface complementarity. All the proteins were found to have good surface complementarity with the SVLAAO; hence it implies all the proteins bind to the SVLAAO strongly. The results of SRB assay exhibited that the IC50 value of Snake venom LAAO on C6 glioma cells was found to be 14.92 nanomolar. A graph was plotted against log concentration and Percentage of the cell death.

Discussion: It was proved that molecular interaction of SVLAAO oxidase with the overexpressed proteins of Glioblastoma resulted in higher surface complementarity, thus has higher binding properties with the selected proteins. The SRB assay conducted after the in-silico study proved that SVLAAO has a IC50 value of 14.92nm. The result of this study correlates with the study conducted using LAAO from Cerastes cerastes snake venom on the U87 glioblastoma cells showed dose dependent cell death from the hydrogen peroxide released.3 In another study done by Costa et al.,2019, it was observed that LAAO from induced cell death in various tumour cells lines like HepG2 and HL60 at low concentrations.4 Hence SVLAAO is proved to possess antitumour activity and can be used in the tumour treatment.

Conclusion: To conclude, the proteins Human dihydropyridines, BAG3 protein, FOXM1B transcription factor Ryanodine receptor 2, Cellular Myc (c-Myc), Human epidermal growth factor receptor (EGFR) and binds with SVLAAO with high surface complementarity. Hence, these proteins can be used as the targets for glioblastoma multiforme treatment. The cytotoxicity assay revealed that SVLAAO can be used as a potent anticancer agent.